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44We CLAIMS

1. A kallikrein inhibiting protein which comprises a non-naturally occurring Kunitz domain, wherein, at each of the residues of said domain corresponding to the below identified residues of BPTI, one of the following allowed amino acids is found:

BPTI
residue #Allowed Amino Acid

10	Asp, Glu, Ala, Gly, Ser, Thr
11	Asp, Gly, Ser, Val, Glu, Leu, Met, Asn, Ile, Ala, Thr
12	Gly, and, if residue 14 or 38 is not Cys, any conservative or semi-conservative substitution for a "normal" conformation Gly as defined in Table 9
13	Arg, His, Pro, Asn, Ser, Thr, Ala, Gly, Lys, Gln
14	Cys, and, if residue 38 is not Cys, any conservative or semi-conservative substitution for Cys
15	Arg, Lys, Ala, Ser, Gly, Met, Asn, Gln
16	Ala, Gly, Ser, Asp, Asn
17	Ala, Asn, Ser, Ile, Gly, Val, Gln, Thr
18	His, Leu, Gln, Ala
19	Pro, Gln, Leu, Asn, Ile
20	Arg, Leu, Ala, Ser, Lys, Gln, Val

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21	Trp, Phe, Tyr, His, Ile
31	Glu, Asp, Gln, Asn, Ser, <u>Ala</u> , <u>Val</u> , <u>Leu</u> , <u>Ile</u> , Thr
32	Glu, Gln, Asp, Asn, Pro, Thr, Leu, Ser, Ala, Gly, Val
33	Phe, Tyr
34	Ser, Thr, Ile, Val, Ala, Asn, Gly, Leu
35	Tyr, Trp, Phe
36	Gly, Ser, Ala
37	Gly, and, if residue 14 or 38 is not Cys, any conservative or semi-conservative substitution for a "normal" conformation Gly as defined in Table 9
38	Cys, and, if residue 14 is not Cys, any conservative or semi- conservative substitution for Cys
39	Gly, Glu, Ala, Ser, Asp.

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2. A kallikrein inhibiting protein which comprises a non-naturally occurring Kunitz domain, wherein, at each of the residues corresponding to the below identified residues, one of the following allowed amino acids is found:

<u>BPTI</u> <u>residue #</u>	<u>Allowed Amino Acid</u>
10	Asp, Glu, Ala, Gly, Ser, Thr
11	Asp, Gly, Ser, Val, Glu, Leu, Met
12	Gly, and, if residue 14 or 38 is not Cys, <u>or</u> any conservative

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semi-conservative substitution
for a "normal" conformation Gly
as defined in Table 9

- 13 Arg, His, Pro, Asn, Ser
- 14 Cys, and, if residue 38 is not
Cys, any conservative or semi-
conservative substitution for
Cys
- 15 Arg, Lys
- 16 Ala, Gly
- 17 Ala, Asn, Ser, Ile
- 18 His, Leu, Gln
- 19 Pro, Gln, Leu
- 20 Arg, Leu, Ala, Ser, Lys, Gln,
Val
- 21 Trp, Phe
- 31 Glu
- 32 Glu, Gln
- 33 Phe
- 34 Ser, Thr, Ile
- 35 Tyr
- 36 Gly, Ser, Ala
- 37 Gly, and, if residue 14 or 38
not Cys, any conservative or
semi-conservative substitution
for a "normal" conformation Gly
as defined in Table 9
- 38 Cys, and, if residue
corresponding to position 14 is
not Cys, any conservative or
semi-conservative substitution
for Cys

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Gly, Glu, Ala.

6 3. The protein of claim 2 wherein, the Kunitz domain is further characterized as follows:

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<u>BPTI</u> <u>Residue No.</u>	<u>Allowed Residue</u>
10	Asp, Glu
11	Asp, Gly, Ser, Val
12	Gly
14	Cys
20	Arg
36	Gly
37	Gly
38	Cys.

4. A plasma kallikrein inhibiting protein which comprises a sequence that is substantially homologous to a reference sequence selected from the group consisting of

Sub B3

KKII/3 #1, KKII/3 #2, KKII/3 #3, KKII/3 #4, KKII/3 #5, KKII/3 #6, KKII/3 #7, KKII/3 #8, KKII/4 #9, KKII/3 #10, KK2/#11, KK2/#13, KK2/#1, KK2/#2, KK2/#3, KK2/#4, KK2/#6, KK2/#7, KK2/#8, KK2/#9, KK2/#10, KK2/#12, AND KK2con1 as defined in Table 2.

C 2 5. A method of ~~preventing~~ or treating a disorder attributable to excessive kallikrein activity which comprises administering, to a human or animal subject who would benefit therefrom, a kallikrein-inhibitory amount of the protein of ^{claim 1} ~~any of claims 1-4~~.

Sub B4 6. A method of assaying for kallikrein which comprises providing

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claim 1
A the protein of ~~any of claims 1-4~~ in labeled or insolubilized form, and determining whether a complex of said protein and the kallikrein in a sample is formed.

Sub B4 cont.
7. A method of purifying kallikrein from a mixture which comprises providing the protein of *claim 1* ~~any of claims 1-4~~ in insolubilized form, and contacting the mixture with said insolubilized protein or analogue so that kallikrein in the mixture is bound.

Add A1

Add B2